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Variations in key genes increase Caucasians' risk of heroin addiction

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(PhysOrg.com) -- Sometimes, small changes do add up. In the case of addictive diseases, tiny variations in a few genes can increase or decrease the likelihood of some people developing a dependency on heroin. Now, by examining a select group of genetic variants in more than 400 former severe heroin addicts, Rockefeller University researchers have identified several genetic variations in American and Israeli Caucasians that influence the risk for becoming addicted to one of the world's most powerful substances.

In a collaborative effort with statistical geneticists and several methadone clinics, scientists led by Mary Jeanne Kreek, head of the Laboratory of the Biology of Addictive Diseases, analyzed 1,350 variations in 130 genes and found nine, from six genes, that were either more or less common in recovering heroin addicts when compared to Caucasians with no history of drug abuse. These small changes in the gene sequences can cause significant changes in protein function that can influence addictive behavior — changes that may affect people of different ethnic background differently.

"The idea of 'personalized medicine' makes this field really exciting but also very complicated," says Orna Levran, a senior research associate in the Kreek laboratory and first author of the study. "Although seven of these variants increase the risk for developing heroin addiction in Caucasians, the same seven may not have the same effect in other populations. So ethnicity and, more precisely, genetic information in each individual may become important factors for treating and

diagnosing addictions to different drugs."

In their analysis, Kreek, Levran and their colleagues looked at a string of letters called nucleotides, the building blocks that make up genes. In each of the six genes, at least one letter is replaced by another, a genetic variation known as a single nucleotide polymorphism, or SNP. The researchers found that all of the single-letter variations exist in parts of the genes that do not translate into proteins but instead may have a regulatory or a structural effect.

Out of the nine SNPs, the group found six in the μ, δ and κ opioid receptors, a finding that reinforces the idea, and many other findings of the Kreek laboratory, that opiate receptors play a major role in severe heroin addiction. The remaining three SNPs were found in genes coding for the serotonin receptor 3B, casein kinase 1 epsilon, which acts as a regulator of the circadian clock genes, and galanin, which modulates appetite and alcohol consumption. This is the first study to show that specific variants in these genes are associated with heroin addiction, explains Levran.

The SNPs in the κ opioid receptor and casein kinase 1 genes were found more in the control group than the heroin addicts' group, suggesting that they conferred protection from heroin addiction — not vulnerability to develop addiction.

"Individually, these SNPs probably have a small effect," explains Levran, "but collectively, we are seeing that they could have a larger effect. One of the goals now is to find all of these gene variants and assess how they influence people of different ethnic backgound."

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